

The Gaines reference is an experimental model with data solely from rats subjected to experimental bilateral hind limb ischemia. This is not a model of immune initiated muscle disease in humans, which is the subject of applicant's claims. Ischemia/reperfusion injury is not the disease model claimed in the present application. This experimental model does not have a disease correlate in humans. Also, Gaines does not disclose or teach the specific TNF antagonists claimed. Thus, applicant's claims are patentably distinguishable.

In the Szalay reference, C2 myoblasts are mouse derived. The experimental model involves the in vitro cell culture of murine cells. There is no support for the extrapolation of these results to human diseases involving inflammation of muscle, or to the immune response affecting muscle. This experimental model is not a mouse model of muscular dystrophy or dermatomyositis. Additionally, the TNF antagonists selected in the claims are not taught by Szalay. Even if they were, the experimental in vitro model utilizing mouse myoblasts cannot be used to predict the results of therapeutic intervention in the human for the treatment of the diseases of consideration in these patent claims. Thus, applicant's claims are patentably distinguishable.

The Person reference discloses a single case report of the use of pentoxifylline for the treatment of dermatomyositis. Pentoxifylline is not one of the TNF antagonists claimed. Further, it has significantly different biochemical and pharmacologic properties from the pure TNF antagonists which are being claimed by applicant.

More specifically, pentoxifylline is a tri-substituted xanthine derivative designated chemically as 1-(5-oxohexyl)-3, 7-dimethylxanthine. It is neither an anti-TNF monoclonal antibody nor an agent containing soluble TNF receptors, as are the therapeutic agents in the submitted claims.

The following is a description of the mode of action of pentoxifylline:

“Pentoxifylline and its metabolites improve the flow properties of blood by decreasing its viscosity. In patients with chronic peripheral arterial disease, this increases blood flow to the affected microcirculation and enhances tissue oxygenation. The precise mode of action of pentoxifylline and the sequence of events leading to clinical improvement are still to be defined. Pentoxifylline administration has been shown to produce dose-related hemorrheologic effects, lowering blood viscosity, and improving erythrocyte flexibility. Leukocyte properties of hemorrheologic importance have been modified in animal and in vitro human studies. Pentoxifylline has been shown to increase leukocyte deformability and to inhibit neutrophil adhesion and activation. Tissue oxygen levels have been shown to be significantly increased by therapeutic doses of pentoxifylline in patients with peripheral arterial disease.”

In the Person reference, it was suggested that the beneficial effect could have been due to the fibrinolytic or viscosity-lowering properties or the TNF-inhibiting properties of the drug. There is no disclosure of using the specific TNF antagonists claimed, which

belong to a completely different class of therapeutic agents. Thus, applicant's claims are patentably distinguishable.

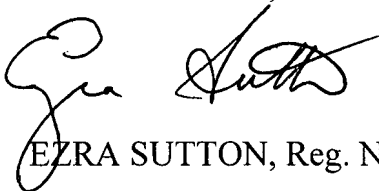
In the Seekamp reference, it states that "in the current study, we have focused on events in lungs occurring during reperfusion of hind limbs...These data suggest that ischemia and reperfusion injury of rat lower extremities causes systemic changes..."

In this study in rats only, the effects of TNF on pulmonary injury was studied. Hind limb ischemia led to systemic changes affecting the lungs. There is no teaching of use for humans, and there is no teaching of the specific claimed TNF antagonists being used. Accordingly, this reference does not constitute prior art to the TNF antagonists claimed.

In summary, for the reasons stated, it is respectfully submitted that the four references do not constitute prior art concerning the specific claims which have been submitted.

Respectfully submitted,

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